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Special thanks to :

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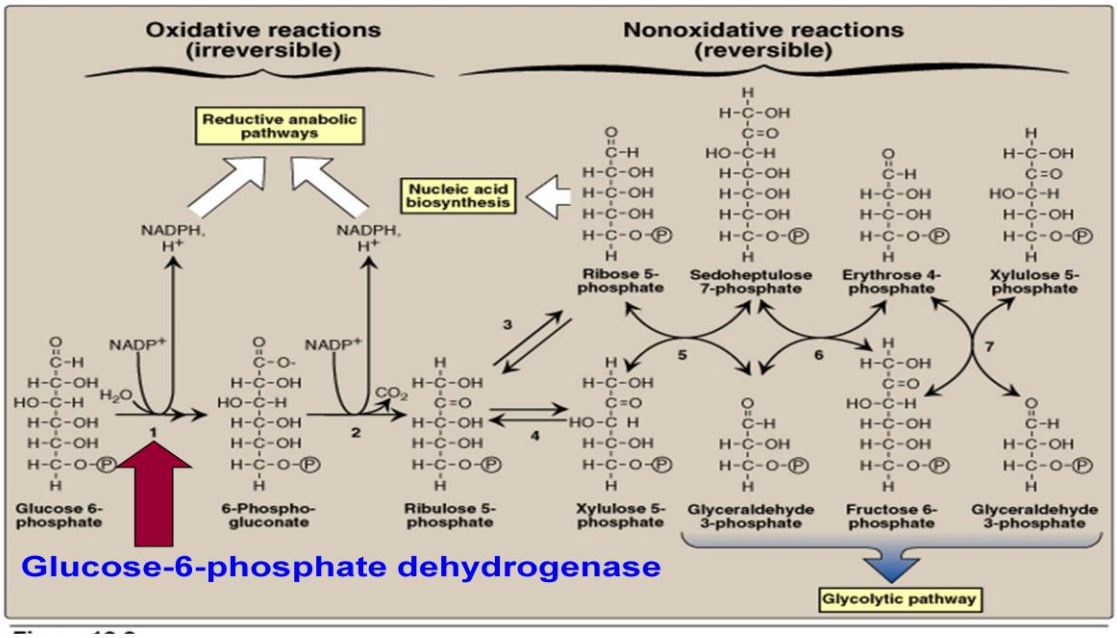
Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency Anemia

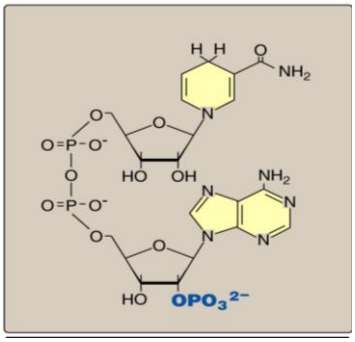
Hexose monophosphate pathway (HMP) or Pentose Phosphate Pathway (PPP):

- **An alternative oxidative pathway for glucose**
- **No ATP production**
- **Major pathway for NADPH production**
- **Produces ribose-5-phosphate for nucleotide synthesis**

Pentose Phosphate Pathway (PPP): "RBc use this pathway "



NADPH:

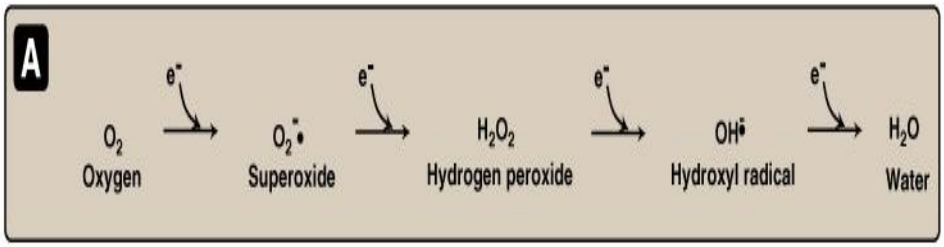


Uses of NADPH

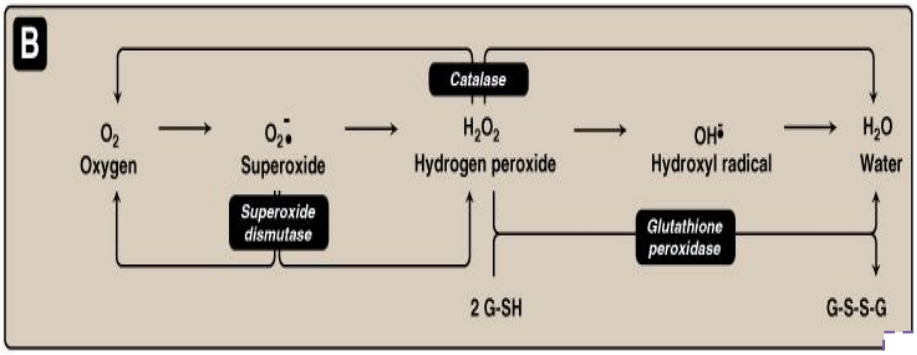
- **Reductive biosynthesis e.g., fatty acid biosynthesis**
- **Antioxidant (part of glutathione system)**
- **Oxygen-dependent phagocytosis by WBCs**
- **Synthesis of nitric oxide (NO)**

Reactive Oxygen Species (ROS):

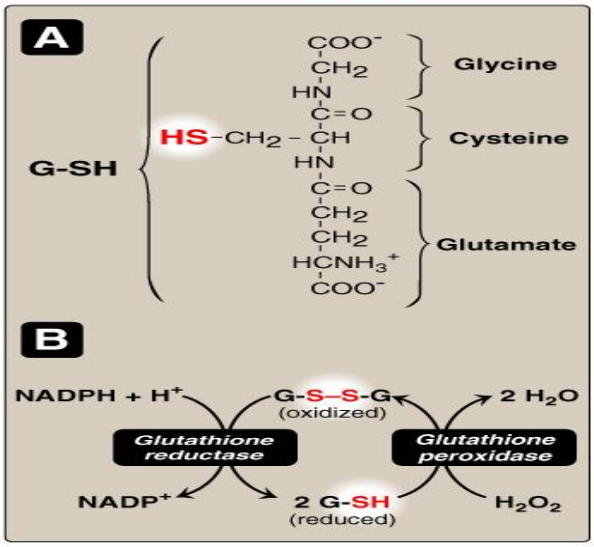
Oxygen-derived Free radicals :e.g., Superoxide and hydroxyl radicals
Non-free radical: Hydrogen peroxide



Antioxidant Mechanisms :



Glutathione System :



Oxidative Stress :

- **Imbalance between oxidant production and antioxidant mechanisms**
- **Oxidative damage to:**
  - **DNA**
  - **Proteins**
  - **Lipids (unsaturated fatty acids)**
- **Oxidative stress and diseases:**
  - **Inflammatory conditions e.g., Rheumatoid arthritis**
  - **Atherosclerosis and coronary heart diseases**
  - **Obesity**
  - **Cancers**
  - **G6PD deficiency hemolytic anemia**

G6PD Deficiency Hemolytic Anemia

- **Inherited X-linked recessive disease**
- **Most common enzyme-related hemolytic anemia**

اذا توقف انتاج

NADP

فان عمليه عكس الاكسده ستتوقف مما ينتج عنه تدمير الخلايا (في هذا الدرس

خلايا الدم الحمراء)

G6PD Deficiency Hemolytic Anemia

مرض يحدث فيه نقص انزيم الـ

G6pD

ـ مما ينتج عنه توقف انتاج ال

NADp

فتتوقف عمليه عكس الاكسده الوحيد ه في خلايا الدم الحمراء مما يسبب تراكم المواد

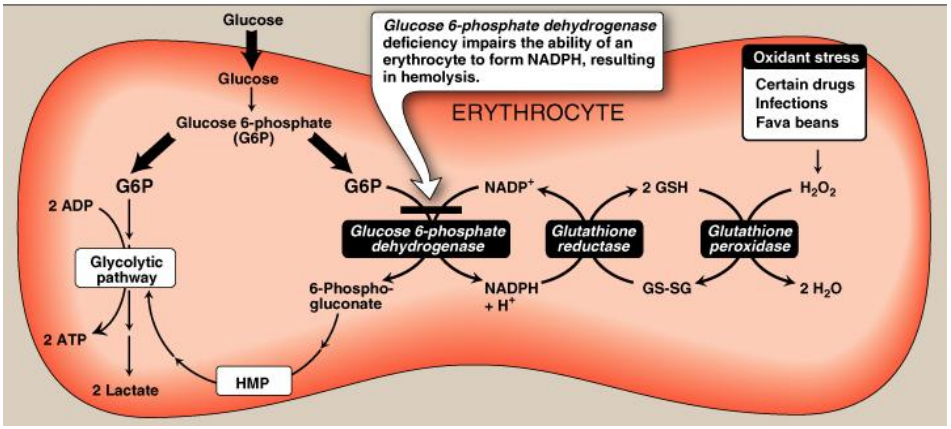
المؤكسده وتحليلها لخلايا الدم الحمراء

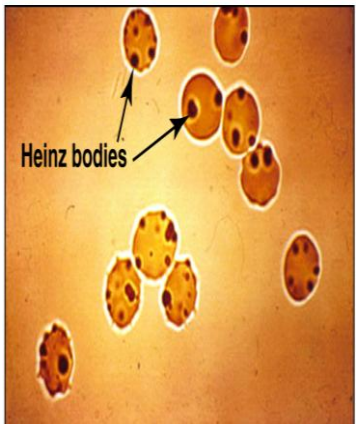
Selinium

ماده غذائيه تساعد على استمرار التفاعل

- **Highest prevalence: Middle East, Tropical Africa**
- **Asia and Mediterranean**
- **~400 different mutations affect G6PD gene, but only some Can cause clinical hemolytic anemia**
- **G6PD deficient patients have increased resistance to Infestation by falciparum malaria**

Biochemical Basis of G6PD Deficiency Hemolytic Anemia:





- **Oxidation of sulfhydryl groups of proteins inside RBCs causes protein denaturation and formation of insoluble masses (Heinz bodies) that attach to RBCs membranes**

- **Although G6PD deficiency affects all cells, it is most severe in RBCs …… Why?**
  B\c Other cells have other sources for NADPH production:
  e.g., Malic enzyme that converts malate into pyruvate

Precipitating Factors for G6PD Deficiency Hemolytic Anemia:

G6PD deficient patients will develop hemolytic attack upon:

- **Intake of oxidant drugs (AAA):**
  Antibiotics e.g., sulfa preparation
  Antimalarial: e.g., Primaquine
  Antipyretics
- **Exposure to infection**
- **Ingestion of fava beans (favism, Mediterranean variant)**
- **Chronic nonspherocytic anemia: Hemolytic attack in absence of precipitating factors. (Severe form due to class I mutation)**

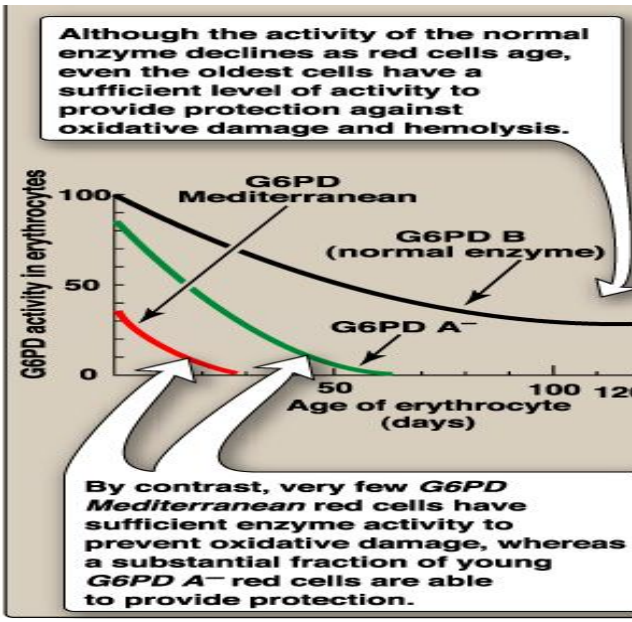
Different Classes of G6PD Deficiency Hemolytic Anemia

Class	Clinical symptoms	Residual enzyme activity
I	Very severe	<2%
II	Severe	<10%
III	Moderate	10–50%
IV	None	60–150%

I > **Hemolytic attack in absence of precipitating factors**

II > Mediterranean Disease

Variant Enzymes of G6PD Deficiency Hemolytic Anemia



G6PD A- (class III):

- Moderate, young RBCs
- Contain enzymatic activity
- Unstable enzyme, but
- Kinetically normal

" kills the big RBC"

G6PD Mediterranean (II)

- Enzyme with normal stability
- but low activity (severe)
- Affect all RBCs (both young and old)
  "the most dangers "

Diagnosis of G6PD Deficiency Hemolytic Anemia

Diagnosis of hemolytic anemia

CBC and reticulocytic count

Screening:

Qualitative assessment of G6PD enzymatic activity(UV-based test)

Confirmatory test:

Quantitative measurement of G6PD enzymatic activity

Molecular test:

Detection of G6PD gene mutation